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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/550,395

09/22/2005

Makoto Sunagawa

2005-1498A

9879

513

7590

11/14/2007

WENDEROTH, LIND & PONACK, L.L.P.

2033 K STREET N. W.

SUITE 800

WASHINGTON, DC 20006-1021

EXAMINER

BERCH, MARK L

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

11/14/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/550,395	<b>Applicant(s)</b> SUNAGAWA ET AL.	
	<b>Examiner</b> /Mark L. Berch/	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14, 16-21 and 24-28 is/are rejected.
- 7) ☒ Claim(s) 15, 22-23 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                        |                                                                   |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/19/2005; 09/22/2005</u> .                                  | 6) <input type="checkbox"/> Other: ____.                          |

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## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6, 8, 14, 17, 18, 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by 5256777.

See column 9, line 45, for G as G2, with Y1 as m-Br. Table III shows the m-Cl, F, Br and I. Table V shows the corresponding para compounds.

Claims 1-3, 8, 12, 17-18, 25-28 are rejected under 35 U.S.C. 102(b) as being anticipated by 4775669.

See Compound 41, columns 57-58, and example 45. This corresponds to G = G1, p-methoxy, Na salt.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-6, 8, 12, 21, 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guthikonda or 4260627.

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In Guthikonda, note compound 56. This corresponds to choice G3 for G, in which A is  $(CH_2)_sNRa(CH_2)_t$ , with  $s=1$ ,  $t=0$  and  $Ra=R^0=H$ . The sole difference is that it has no second substituent on the phenyl, i.e. it has  $Y_2=H$ , whereas the rejected claims call for  $Y_2=methyl$ . It is to be noted that this compound is clearly a very desirable one. Its DHP-1 susceptibility is lower than any other compound tested in the reference. Further, it is a very potent compound compared with thienamycin.

Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, “The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a *prima facie* case of obviousness of a compound may rest.” The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 247; *Ex parte Henkel*, 130 USPQ 474; *In re Jones*, 74 USPQ 152, 154; *In re Herr*, 134 USPQ 176; *Ex parte Dibella*, 157 USPQ 59; *In re Zickendraht*, 138 USPQ 22; *Ex Parte Fischer*, 96 USPQ 345; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39; *In re Bowers and Orr*, 149 USPQ 570. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. As was stated directly in *THE GENERAL TIRE & RUBBER COMPANY v. JEFFERSON CHEMICAL COMPANY, INC.*, 182 USPQ 70 (1974): “If any structural change is obvious to one skilled in the art, a substitution of the next higher homolog would seem to be.” Note also *In re Jones*, 21 USPQ2d

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1942, which states at 1943 “Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness”; one of those listed is “adjacent homologues and structural isomers”. Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states “a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds.” Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, “Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.” See also MPEP 2144.09, second paragraph.

Claims 1, 5-6, 8, 12, 21, 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over 5034385.

In this reference, note compound 14. This corresponds to choice G3 for G, in which A is  $(CH_2)_sNRa(CH_2)_t$ , with  $s=1$ ,  $t=0$  and R0 is Formula 3, where  $m=0$  and R3b is heteroaryl (here, pyridyl). The compound is the K salt of the acid. It is missing only the methyl and is thus obvious for reasons set forth in the above rejection.

Claims 1, 5-6, 8, 12, 21, 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4260627 in view of Guthikonda.

In 4260627, see table 5, compound 26. This corresponds to choice G3 for G, in which  $(CH_2)_sNRa(CH_2)_t$ , with  $s=1$ ,  $t=0$  and  $Ra=R^0=H$ ,  $Y2=CH_3$ . The sole difference is that it has the 1-methyl substituent, whereas applicants do not have the 1-methyl substituent.

First, Guthikonda provides motivation to select compound 26. The aminomethyl-phenyl substituent is taught by Guthikonda to be the best substituent, as was discussed above. Thus, one is

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motivated to pick a compound from the primary reference with that structural feature. Second, Guthikonda provides a compelling motivation to modify the compound by removing the 1-methyl feature. The Guthikonda reference states, page 875, column 2, second full paragraph, "in the 2-aryl cases examined to date ... diminution of activity and metabolic stability by 1-substitution, is observed." That is, in the 2-aryl compounds, which are the subject of these claims, removing the 1-methyl group produces better compounds. Thus, in a comparison of compound 56, the closest species to the claims as discussed above, and the corresponding 1-methyl derivative 51, one sees that 56 has better DHP-I stability, and is more potent as an antibacterial in 7 of 8 comparisons. This provides a specific motivation to remove the 1-methyl group.

Claims 4-6, 13, 16 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4775669.

See Compound 41, columns 57-58. This corresponds to G = G1, p-methoxy, Na salt, as discussed above. Choice G2 provides Y1 as ethoxy, which is a homolog of the methoxy of the prior art compound. These render claims 4, 13, 16 obvious. In addition, note Table V, starting in column 96, compounds 3, 6-8, 10, 50, 54, 118, 123, which correspond to choice G3 for G, in which A is  $(CH_2)_sNRa(CH_2)_t$ , with  $s=1$ ,  $t=0$  and  $Ra=R^0=H$  or alkyl. These render 5-6, and 21 obvious, again as homologs. Similar are 11 and 13, corresponding to A as methylene, R0 as choice 3. Note also compound 49, which corresponds to choice G2, except that G2 has a methyl on the phenyl ring which this compound lacks, so that this is also a homolog. The homologs are obvious for reasons set forth above.

Claims 1, 4, 14, 17-18, 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4203902.

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See compound 9, which corresponds to choice G2, except that G2 has a methyl on the phenyl ring which this compound lacks, so that this is also a homolog. The homologs are obvious for reasons set forth above.

Claims 6-7, 9-10, are rejected under 35 U.S.C. 103(a) as being unpatentable over 5256777, 4775669, Guthikonda, 4260627, 5034385 or 4203902, in view of 4464299, 4429128 4223038, 5055463 or 5869477.

The primary references are applied as above. These claims are embrative of the pivaloyloxymethyl ester form of the carbapenem, as opposed to the acids or salts of the carbapenems as shown in the primary references. However, the pivaloyloxymethyl is well known in the carbapenem art as being a conventional and even preferred choice for the ester, as is demonstrated in the secondary references. See 4464299, claim 10; 4429128 claim 9; 4223038, claim 10; 5055463, claim 6; 5869477 claim 5.

Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over 5256777, 4775669, Guthikonda, 4260627, 5034385 or 4203902, in view of 4223038, 4350703, 4464299, 5055463, or 4536335.

The primary references are applied as above. These claim is embrative of the phthalidyl ester form of the carbapenem, as opposed to the acids or salts of the carbapenems as shown in the primary references. However, the phthalidyl is well known in the carbapenem art as being a conventional and even preferred choice for the ester, as is demonstrated in the secondary references. See 4223038, claim 9; 4350703, claim 10; 4464299, claim 6; 5055463, claim 6; 4536335, claim 13.

#### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is

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appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-12, 19, 25-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 7205291. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no line of demarcation between the two cases. Patent claim 1, where E is benzene, corresponds to A is  $(CH_2)_sO(CH_2)_t$ , with  $s=1$ ,  $t=0$  and R0 is Formula [2]. See e.g. patent column 43, species 4 and 5, which fall within the rejected claims.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-12, 19-20, 24-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Me must be defined as methyl or metal.
2. In next to last line of claim 1, “azepam” cannot be right. Was “azepane” intended?



***Claim Objections***

**Claims 8, and 24-28 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on a multiply dependent claim, e.g. claim 6. See MPEP § 608.01(n).**

**Claim 1 has a period in the middle; see top line of page 121.**

**Claim 7 cannot depend on both claim 1 for Formula I and also claim 4 (actually, claim 6) for Formula [4].**

**Claims 15, 22, 23 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.**

**Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Mark L. Berch/ whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.**

**If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.**

**Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.**

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**/Mark L. Berch/  
Primary Examiner  
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